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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/510,237	10/14/2004	Yasushi Yamazoe	260297US0XPCT	7042

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EXAMINER	
MCGILLEM, LAURA L	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 11/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/510,237	YAMAZOE ET AL.	
	Examiner	Art Unit	
	Laura McGillem	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 October 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/3/04, 2/2/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Priority

It is acknowledged that the instant application is a National stage application of PCT/JP03/04761, filed 4/15/2003 and receives priority to Japanese patent 2002112364, filed 4/15/2002.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 3, 5 and 7 are vague and indefinite because they recite a vector comprising a reporter gene and PXR binding regions as part of a CYP3A gene, but it is not clear whether or not the reporter gene is operably linked to the CYP3A gene.

Claims 2, 4, 6 and 8 are vague and indefinite because they recite "7.7k" and "7.4k" and it is not clear what "k" denotes. It the Applicants intend "k" to be an abbreviation for kilobase, it would be remedial to change "7.7k" to "--7.7kb--" for example. Claims 2, 4, 6 and 8 are vague and indefinite because they recite, a "362 (ER-6) region", and it is unclear what is meant by "362".

Claims 6 and 8 are vague and indefinite because they respectively recite the phrases "the method according to claim 5" and "the method according to claim 7" and

claims 5 and 7 are drawn to reagents and not methods. Therefore, it is not clear to what methods claims 6 and 8 refer.

Claims 1, 3, 5 and 7 are vague and indefinite because they recite the phrase "at least 3 human PXR binding regions falling within an untranslated region of a human CYP3A gene" and it is not clear if the claimed vector comprises only the "at least 3 human PXR binding regions" or if the claimed vector comprises the "at least 3 human PXR binding regions" in the context of the untranslated region of the human CYP3A gene.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 3, 4, 7 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Goodwin et al (Mol. Pharm. 1999, Vol. 56, pp 1329-1339, of record).

Goodwin et al teach a method to measure CYP3A4 induction by rifampicin, indicated by luciferase expression, comprising the use of a plasmid construct p3A4-362 (7836-7208ins) comprising a luciferase reporter gene and portions of the promoter regions located at bases (-7836 to -7208) and (-362 to +53) of the human CYP3A4 gene. These promoter regions comprise PXR response elements known as dNR1, dNR2, MIE and ER-6 (see page 1330, right column, last paragraph, page 1333, Figure

4, and page 1335, left column, 1st full paragraph, in particular), which reads on a plasmid vector comprising a detectable reporter gene and at least 3 human PXR binding regions falling within an untranslated region of a human CYP3A gene. Goodwin et al also teach that the plasmid construct p3A4-362 (7836-7208ins) was transfected into a human liver cell line (HepG2) in order to examine CYP3A4-luciferase induction by rifampicin, RU486, dexamethasone, rifampicin, phenobarbitol, metyrapone, phenytoin and pregnenolone 16α-carbonitrile or clotrimazole (see page 1335, right column, 2nd full paragraph, for example) which reads on a method of measuring human CYP3A inducibility on administration of a test drug by culturing human cells in a medium containing the test drug, the transformed human cell being created by means of transfer of DNA in a plasmid vector and then measuring the expression level of the reporter gene and a reagent for measuring CYP3A inducibility comprising said cells.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 5 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goodwin et al (Mol. Pharm. 1999, Vol. 56, pp 1329-1339, of record), in view of Furukawa et al (J. Biochem. 2002, Vol.131, pp.71-78, of record).

Applicants claim a method for measuring human CYP3A induction upon administration of a test drug, comprising administering a test drug to a non-human animal, or a population of cultured human cells, infected with viruses (A) and (B); virus (A) being an adenovirus vector comprising a detectable reporter gene and at least 3 human PXR binding regions falling within an untranslated region of a human CYP3A gene, and virus (B) being an adenovirus vector comprising a human PXR cDNA; and determining the expression level of the reporter gene.

Goodwin et al teach a plasmid construct p3A4-362 (7836-7208) comprising a luciferase reporter gene and portions of the promoter regions located at bases (-7836 to -7208) and (-362 to +53) of the human CYP3A4 gene. These promoter regions comprise PXR response elements known as dNR1, dNR2, MIE and ER-6 (see page 1330, right column, last paragraph, page 1333, Figure 4, and page 1335, left column, 1st full paragraph, in particular). Goodwin et al also teach an hPXR expression vector which was cotransfected into a human liver cell line (HepG2) in order to examine CYP3A4 induction by rifampicin, which was indicated by luciferase expression (see page 1335, right column, 2nd full paragraph, for example).

Goodwin et al do not teach that the DNA constructs are present in adenoviruses that are being used as vectors.

Furukawa et al teach an adenovirus reporter vector comprising a luciferase reporter gene and a portion of the promoter region of the human CYP3A4 gene (-362 to +11 nt), which includes an ER-6 PXR binding region (see page 72, left column, last paragraph, for example). The CYP3A4 adenoviral reporter vector was used to infect

cultured HepG2 liver cells and mice in order to determine the effect of drugs such as dexamethasone, rifampicin or clotrimazole on CYP3a4 induction driven reporter activity (see page 74,1st full paragraph, for example).

It would have been obvious to one of ordinary skill in the art to modify the teaching of Goodwin et al to use an adenoviral vector to deliver CYP3A4 to cells and non-human animals because Furukawa et al suggest that adenoviral vectors may alleviate problems with *in vitro* drug effect studies such as alteration in expression profiles of drug-metabolizing enzymes when studied *in vitro* with immortalized cultured cells, and alteration of gene activation by artificial promoters (see page 71, right column, 1st full paragraph, for example). The motivation to do so would be the benefit of being able to more accurately determine the effect of a test drug on human CYP3A inducibility in cells and in non-human animals. There is reasonable expectation of success in using an adenoviral reporter vector to introduce CYP3A4 constructs because this has worked previously in the cited techniques.

Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time the invention was made, it must be considered that said ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura McGillem whose telephone number is (571) 272-8783. The examiner can normally be reached on M-F 8:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Laura McGillem, PhD
10/27/2005

DAVID GUZO
PRIMARY EXAMINER